

CLAIMS:

1. An isolated fragment of a natural cytotoxicity receptor of an NK cell, comprising the linker peptide connecting the extracellular domain of the receptor to the transmembrane portion of the receptor, said peptide exhibiting at least one activity selected from binding to a viral infected cell or a tumor cell.
2. The peptide of claim 1 comprising at least one glycosylated residue.
3. The peptide of claim 1 wherein the natural cytotoxicity receptor of the NK cell is selected from NKp46 and NKp44.
4. An isolated fragment of the human NKp46 receptor comprising the amino acid sequence as set forth in SEQ ID NO:3, the peptide having the ability to bind to target cells selected from viral-infected cells and tumor cells, an active fragment, an isoform, an analog or a derivative thereof, with the proviso that said peptide is other than SEQ ID NOS:1 and 2.
5. The peptide of claim 4 wherein the target cell is of a warm-blooded vertebrate.
6. The peptide of claim 5 wherein the target cell is of human origin.
7. The peptide of claim 4 comprising a minimal epitope of NKp46 receptor having ability to bind to viral-infected cells.
8. The peptide of claim 7 comprising a glycosylated residue corresponding to threonine at position 225 of isoform a of the human NKp46 receptor.
9. The peptide of claim 7 wherein the glycopysylation comprises sialic acid.
10. The peptide of claim 4 comprising from about 10 to 100 amino acid.
11. The peptide of claim 4 comprising from about 30 to 60 amino acids.
12. An isolated fragment of the human NKp44 receptor comprising the amino acid sequence as set forth in any one of SEQ ID NOS:6 and 7, the peptide having the ability to bind to target cells selected from viral-infected cells and tumor cells, an active fragment, an analog or a derivative thereof, with the proviso that said peptide is other than SEQ ID NOS:4 and 5.
13. The peptide of claim 16 wherein the target cell is of a warm-blooded vertebrate.

14. The peptide of 17 wherein the target cell is of human origin.
15. The peptide of claim 18 comprising a minimal epitope of NKp44 receptor having ability to bind to viral-infected cells.
16. The peptide of claim 19 comprising at least one glycosylated residue.
- 5 17. The peptide of claim 20 comprising a plurality of glycosylated residues.
18. The peptide of claim 16 comprising from about 10 to 100 amino acid.
19. The peptide of claim 16 comprising from about 30 to 60 amino acids.
20. A fusion protein comprising a peptide according to any one of claims 1-19, other than the fusion proteins of SEQ ID NOS:13-18.
- 10 21. The fusion protein of claim 20 manufactured by recombinant DNA technology or chemical synthesis.
22. The fusion protein of claim 21 comprising a peptide covalently conjugated to a molecule selected from an immunoglobulin (Ig) molecule or a fragment thereof, and a cytotoxic substance.
- 15 23. The fusion protein of claim 22 wherein the peptide is covalently conjugated to the Fc fragment of said immunoglobulin molecule.
24. A pharmaceutical composition comprising as an active ingredient a peptide according to any one of claims 1-19.
- 20 25. The pharmaceutical composition of claim 24 further comprising pharmaceutically acceptable diluents, carriers or excipients.
26. A pharmaceutical composition comprising as an active ingredient a fusion protein according to any one of claim 20-23.
27. The pharmaceutical composition of claim 26 further comprising pharmaceutically acceptable diluents, carriers or excipients.
- 25 28. Use of the peptide of any one of claims 1-19 in the preparation of a pharmaceutical composition useful for exerting cytotoxic effect on viral-infected cells.

29. Use of the peptide of claim 4 in the preparation of a pharmaceutical composition useful for exerting cytotoxic effect on viral-infected cells.

30. Use of the peptide of claim 12 in the preparation of a pharmaceutical composition useful for exerting cytotoxic effect on viral-infected cells.

5 31. Use of the peptide of claim 17 in the preparation of a pharmaceutical composition useful for exerting cytotoxic effect on viral-infected cells.

32. Use of the peptide of any one of claims 1-19 in the preparation of a pharmaceutical composition useful for exerting cytotoxic effect on tumor cells.

10 33. Use of the peptide of claim 4 in the preparation of a pharmaceutical composition useful for exerting cytotoxic effect on tumor cells.

34. A method for treating a viral disease in a subject comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising as an active ingredient a peptide according to any one of claims 1-19.

15 35. A method for treating a viral disease in a subject comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising as an active ingredient a peptide according to claim 4.

20 36. A method for treating a viral disease in a subject comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising as an active ingredient a peptide according to claim 12.

37. A method for treating a viral disease in a subject comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising as an active ingredient a peptide according to claim 17.

25 38. A method for treating a malignant disease in a subject comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising as an active ingredient a peptide according to any one of claims 1-19.

39. A method for treating a malignant disease in a subject comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition comprising as an active ingredient a peptide according to claim 4.

40. A monoclonal antibody (mAb) specific for an epitope in the distal domain of NKp46 receptor.

41. The monoclonal antibody of claim 40, wherein said antibody is produced by a hybridoma denoted as 461-G1.

42. The monoclonal antibody of claim 40, wherein the antibody is capable of selectively removing NKp46-positive cells.

43. A method for selective removal of Natural Killer (NK) cells from a biological sample comprising contacting the biological sample with an antibody specific for an epitope of NKp46 receptor or immunoreactive fragments thereof, under condition appropriate for immune complex formation, and removing the immune complex formed from the biological sample.

44. The method of claim 43, wherein said biological sample is selected from the group consisting of peripheral blood, plasma, bone marrow aspirates, lymphoid tissues, or cells isolated from plasmapheresis.

45. The method of claim 44, wherein said biological sample is derived from a subject who would benefit from a decrease in NK cell activity.

46. The method of claim 36, wherein said subject is a recipient of transplant tissue, a subject suffering from an autoimmune disease, or a subject requiring gene therapy treatment using a viral vector.

47. A variant polypeptide comprising NKp46 receptor polypeptide or an active fragment thereof having at least a single amino acid substitution in an epitope required for the recognition of viral-infected cells or tumor cells.

48. The variant polypeptide of claim 38, wherein the single amino acid substitution of NKp46 isoform a is Threonine 225 replaced by Serine.